



## Value of Monitoring Serum Immunoglobulins Questioned

Our journal club's review of the recent article by Szczeklik al. (*EHP* 102:302–304) found fault on many levels, especially with the concluding recommendation. It would be neither practical nor useful for workers exposed chronically to PAHs to have serum immunoglobulin levels monitored regularly. The use of cross-sectional data regarding serum immunoglobulin levels for detecting immune competence is not clinically sound. Except in patients with congenital deficiencies, there is no correlation between these levels and resistance to infection. There is no basis to compare mean values within the statistically normal range in the expectation that changes reflect immunosuppression. If humoral immune competence is to be evaluated, a useful test involves assessment of the dynamic response to a particular antigen challenge. This biological function has been shown to diminish following *in vitro* exposure to benzo[*a*]pyrene, but there is little basis for linking this effect to cancer consequences.

Polycyclic aromatic hydrocarbons are not clinically linked to the development of opportunistic infections, the most significant sign of immune suppression. Even if this type of immune deficit had been shown in these workers, there is no basis to make the assertion that humoral immunocompetence has any role in carcinogenesis. Cancer immune surveillance is most significantly accomplished by tumor-infiltrating and T-cell lymphocytes, especially CD8 cells and the helper CD4 cells. Patients with early and even late-stage cancer usually have normal or elevated levels of total serum immunoglobulin, the opposite effect of Szczeklik's workers.

Lastly, the paper's own data refute the routine monitoring of exposure with this biological tool. No correlation with duration or magnitude of exposure was identified among these heavily exposed workers. The published graph of the groups intensely overlapping IgG results provides a strong argument against any use of this test in worker monitoring.

Critical scrutiny is necessary before introducing routine clinical tests, especially in workplace health and safety. In the setting described in the Szczeklik paper, expenditures on exposure evaluation and reduction by traditional industrial hygiene methods would be more useful than any biological monitoring. In the clinical arena, education and counseling to decrease the

workers astonishing 75% prevalence of active smoking would be essential.

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## Response

Greenberg and Tippens's assertion that measurement of serum immunoglobulins is of little value in testing humoral immunity flies in the face of well-established clinical knowledge. So does the statement that "Except in patients with congenital deficiencies, there is no correlation between these [serum immunoglobulin] levels and resistance to infection." Examples refuting the latter statement include certain forms of late-onset hypogammaglobulinemia, also called common variable immunodeficiency, malnutrition, Epstein-Barr virus infection, and depression of serum immunoglobulins caused by high doses of cyclophosphamide or by corticosteroid use in nonatopic (infectious) asthma.

Greenberg and Tippens declare: "there is no basis to compare mean values" between the two groups. Why not? The groups were well matched, differing only with regard to chronic PAH exposure. Mathematical analysis revealed that mean serum IgG and IgA differed with high statistical probability ( $p < 0.01$ ) between the groups. Moreover, in the group of coke-oven workers, 21.5% of the subjects had IgG levels  $\leq 1000$  mg/dl, and 5% had  $< 700$  mg/dl. Such a distinct depression of serum immunoglobulin would be of concern to any clinician.

We have demonstrated for the first time in humans that chronic exposure to high PAH concentrations leads to humoral immunosuppression. Based on this finding, we have suggested that workers exposed chronically to high PAH concentrations should have serum immunoglobulins monitored regularly. A similar conclusion was recently reached by Saboori and Newcombe (1), based on their comprehensive review of the existing evidence of immunotoxic effects of PAH in animal studies. The fact that we have not observed a correlation between the length of exposure and serum immunoglobulin levels does not detract from the value of immunoglobulin monitoring. Other factors that we did not evaluate, such as genetic susceptibility or personal exposure, most likely had a significant effect on the immune response.

We agree with Greenberg and Tippens that there is no proof that immunosuppression, as demonstrated by us, is causally related to the high rate of malignancy among coke-oven workers. We did not make such an assertion, the proof of which would require prospective studies. We share the view of Greenberg and Tippens that cigarette smoking does not promote health and should be counteracted.

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## REFERENCE

1. Saboori AM, Newcombe DG. Environmental chemicals with immunotoxic properties. In: Clinical immunotoxicology (Newcombe DS, Rose NR, Bloom JC, eds). New York: Raven Press, 1992;382.

## PAH Cleanup in Illinois

The article entitled "Establishing Generic Remediation Goals for the Polycyclic Aromatic Hydrocarbons: Critical Issues" by Peter K. LaGoy and Thamsen C. Quirk in the April 1994 edition of *Environmental Health Perspectives* (102: 348–352) reported soil remediation goals proposed by various state regulatory agencies, including Illinois, for carcinogenic PAHs. The objectives reported in this article are incorrect. The cleanup objectives reported by the authors do not match those in Table 2 of the 1991 reference which they cite. An updated version of the reference cited by the authors was published February 1993. A copy of those soil cleanup objectives and acceptable detection limits is included as Table 3 of the 1993 document. However, there is currently a regulatory proceeding before the Illinois Pollution Control Board that may or may not change the 1993 objectives.

We are concerned that the article portrays the Illinois approach as simplistic by setting one cleanup objective for the carcinogenic PAHs, when, in fact, there is a great deal of support behind these objectives. Please print this letter in order to clear up any misunderstanding among the regulated community.

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